36. (Amended) The method of claim 31, further comprising eluting the poly(A) mRNA from the non-reacting structure with an eluting solution with low ionic strength.

These amendments are illustrated in Appendix A attached hereto.

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-61 were originally filed in the application. In a Restriction Requirement mailed on 1 October 2002, the Applicant was requested to choose between two groups of inventions. Applicant traversed the restriction in a Response filed on 7 November 2002. In the present Office Action, the Examiner reconsidered the issue, which Applicant's representative appreciates, and re-joined the groups. Thus, claims 1-61 were pending prior to the Office Action dated 30 January 2003.

Claims 1, 13, 14, 17, 20, 24, 26, 29, 31, and 34-36 have been amended to clarify the invention and provide the proper antecedent basis for the claims. Support for the amendments may be found throughout the specification, for example, at page 5, lines 18-23. No new matter has been added. For the Examiner's convenience, the pending claims are attached hereto as Appendix B.

B. Claims 1-5, 10-15, 18, 22-26, 28-30, 31, 33-42, 46, 47, 50, 53, 54, 56-58, and 61 Are Not Anticipated by Kearney *et al.*

The Action rejects claims 1-5, 10-15, 18, 22-26, 28-30, 31, 33-42, 46, 47, 50, 53, 54, 56-58, and 61 under 35 U.S.C. § 102(b) as anticipated by the reference of Kearney *et al.* (U.S. Patent No. 5,759,777) ("Kearney patent"). It contends that the Kearney patent teaches a method

for isolating poly(A) RNA comprising using a mixture of tetrtamethylammonium chloride (TMAC) or tetraethylammonium chloride (TEAC) as an isostabilizing agent in a mixture with guanidinium. That reference is also alleged to teach the following: incubating the composition for at least four hours (col. 14, line 56); heating the mixture at temperatures ranging from 40 °C to 95 °C; various concentrations of TMAC, including 1 M to 3 M (col 36, col. 12, lines 20-25, and cols. 8-9); and, derivatization with biotinylated labels (col. 23, line 18). Applicant respectfully traverses this rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The Kearney reference does not anticipate the claims of the invention because it does not teach an element of the claims. Claim 1 recites:

> A method for purifying poly(A) mRNA from a sample comprising:
>
> a) incubating a composition comprising:
>
> i) the sample, wherein the sample includes poly(A) mRNA;
>
> ii) a poly(dT) or poly(U) nucleic acid molecule; and
>
> iii) an isostabilizing agent, wherein the isostabilizing agent is tetramethylammonium chloride (TMAC) or tetraethylammonium chloride (TEAC),
>
> under conditions allowing poly(A) mRNA to hybridize with the poly(dT) or poly(U) nucleic acid molecule; and
>
> b) isolating the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA.

The Kearney patent fails to teach that the sample includes either poly(A) RNA (claim prior to amendment) or poly(A) mRNA (claim after amendment). The claimed method is directed toward purifying poly(A) mRNA from a sample, and therefore, the sample is understood to include poly(A) mRNA. Moreover, the claim recites, for clarification purposes, that the sample includes poly(A) mRNA. However, the Kearney patent does not describe any method involving poly(A)

RNA or poly(A) mRNA. No *mention* is made anywhere of mRNA, poly(A) RNA, mammalian cells or any eukaryotic cell or extract. In fact, as the examples make clear, the Kearney patent is concerned with identifying *microbial* nucleic acids in a sample. The Kearney patent states at col. 28, lines 39-40, "The experiments reported above all involved the detection of targets from bacterial cell extracts." In subsequent experiments, extracts from *E. coli*, listeria. *Salmonella typhimurium*, and *Neisseria gonorrhoeae* were used. None of these extracts contain poly(A) mRNA, nor did any experiments involve adding such nucleic acids to the extracts.

At best, the Kearney patent discloses in col. 6 that poly-dA-tailed oligonucleotides can be used. A poly-dA-tailed oligonucleotide is not a poly(A) RNA or poly(A) mRNA because it is a deoxyribonucleic acid. Therefore, it is clear that the cited reference does not teach every element of the claimed method; accordingly, it cannot anticipate the method claims. Applicant respectfully requests the rejection be withdrawn.

C. Claims Are Not Rendered Obvious by the Kearney Patent, Aviv *et al.*, Jacobs *et al.* or Conlan *et al.*

1. Claims 2-4, 16, 17, 39-41, 45, 48, 49, and 52 Are Not Rendered Obvious by the Kearney Patent

The Action rejects claims 2-4, 16, 17, 39-41, 45, 48, 49, and 52 under 35 U.S.C. §103(a) as being unpatentable over the Kearney patent. It acknowledges that the Kearney patent fails to disclose the specific ranges of TEAC and TMAC concentrations of the rejected claims, but argues it would have been *prima facie* obvious to one of ordinary skill in the art to arrive at those concentrations. The Kearney patent is said to teach concentration ranges of 1.4 M to 5 M. The Action further argues that the case of *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955) (cited in MPEP § 2144.05), says that differences in concentration or temperature do not support the

patentability of an invention encompassed in the prior art unless there is evidence that these parameters are critical. Applicant respectfully traverses this rejection.

As discussed above, the Kearney patent does not teach or disclose incubating a sample that has poly(A) mRNA with TMAC or TEAC. Furthermore, the Kearney patent does not render obvious the claimed invention for several reasons. As will be discussed below, the Kearney patent does not render obvious the claimed invention because 1) it does not teach each element of the method claims, 2) it does not provide a reasonable expectation of success, 3) it does not divulge the problem associated with mRNA isolation that the inventor discovered and thus, provides no motivation for its combination with a poly(A) mRNA isolation reference, and 4) it teaches away from the claimed invention.

The Kearney patent is generally concerned with the detection of microbial organisms in a sample and the development of improved general hybridization conditions. In contrast, the present invention concerns isolation of mRNA and reductions in rRNA contamination in the isolated mRNA. As the Declaration of Richard C. Conrad ("Declaration") (Appendix C) states, the invention is "based on [the] discovery that some problems with mRNA isolation stems from rRNA carryover that is based not on rRNA interactions with the targetting molecule, such as oligo-dT, but on rRNA interactions with mRNA. Declaration at ¶ 4.

"[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is *part* of the 'subject matter as a whole,' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." MPEP § 2141.02 (citing *In re Sponnoble*, 405 F.2d 578, 585, 160 U.S.P.Q. 237, 243 (C.C.P.A. 1969)). In this case, the discovery of the source of the problem was only half the battle because the remedy itself was not obvious. While

TEAC and TMAC were known to stabilize A:T basepairing, one would have expected that those agents would also stabilize any A:T basepairing between rRNA and whatever nucleic acid to which it might be sticking; however, as the Declaration indicates, the inventor "believe[s] the TEAC and TMAC reduce basepairing between the rRNA and mRNA, as well as rRNA and a poly(T) or poly(U) nucleic acid that might be employed to hybridize with the mRNA." Declaration at ¶ 5.

evidence on the record. See 1160 45 - 55

To render claims obvious, the cited references must reveal that in so making or carrying out, those of reasonable skill would have a reasonable expectation of success. *In re Vaeck*, 20 U.S.P.Q. 2d 1438, 1443 (Fed. Cir. 1991) *citing In re Dow Chemical Co.*, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). There was no reasonable expectation of success with respect to the claimed invention because one would not expect that stabilization of A:T basepairing would effect an increase of mRNA yield with a concomitant decrease in rRNA contamination, as is described in Examples 1 and 2 and on page 27, lines 20-25 of the specification. Moreover, the extent of the success would not have been expected. Therefore, one would not consider using the claimed method in the context of mRNA isolation.

Another basis for the argument that the claimed invention is not obvious is the fact that the technology of mRNA isolation using poly(T)-cellulose or poly(U) cellulose and the technology of using TEAC or TMAC as a stabilizing agent have been known to those of skill in the art for 30 years, as the Action points out on page 5. The references of Aviv *et al.*, "Purification of biologically active globin messenger RNA by chromatography on oligothymidylic acid-cellulose," *Proc. Nat'l. Acad. Sci. U.S.A.* **69**(6):1403-12 (1972) ("Aviv reference") (cited in a subsequent obviousness rejection), and Melchior *et al.*, "Alteration of the relative stability of dA-dT and dG-dC base pairs in DNA," *Proc. Nat'l. Acad. Sci. U.S.A.*

70(2):298-302 (1973) ("Melchior reference") (Appendix D) illustrate the use of these technologies individually. Even though these technologies are used all the time by persons skilled in the art, no one has employed the two technologies together before the invention in this application. Furthermore, it cannot be disputed that mRNA isolation is a technique also frequently used by scientists, and therefore, an improved technique for isolating mRNA was surely desirable. A person of ordinary skill in the art had the reason to achieve the claimed invention, but did not do so. This further supports Applicant's claim of nonobviousness.

As discussed with respect to the anticipation rejection, the Kearney patent does not describe or suggest the use of TMAC or TEAC in the context of poly(A) mRNA isolation. Even if a reference were cited regarding poly(A) mRNA, there would be not motivation or suggestion to combine the Kearney patent with a reference discussing poly(A) mRNA isolation because it was not known, until the instant specification, that TMAC or TEAC would have the effect of reducing the amount of contaminating rRNA in a sample.

Moreover, the teachings of the Kearney patent suggest *not* using TMAC or TEAC to isolate mRNA while reducing the amount of rRNA. The Kearney patent employs TMAC or TEAC in the context of capturing a complex that includes rRNA in a number of examples in its specification. In Table 1, up to 100% of a complex including rRNA was captured. In Table 6, the signal to noise ratio for a reagent comprising 4M TMAC is 120:1 and 56:1 using an rRNA riboprobe. This illustrates that the Kearney patent teaches the use of TMAC and TEAC if hybridization of rRNA is desired. In the methods of the present invention, rRNA is specifically not desired. Thus, the Kearney patent teaches away from the claimed invention. According to established patent law, "The relevant portions of a reference include not only those teachings which would suggest particular aspects of an invention to one having ordinary skill in the art, but

also those teachings which would lead such a person away from the claimed invention." *In re Mercier,* 185 U.S.P.Q. 774, 778 (C.C.P.A. 1975). In this case, aspects of the Kearney patent clearly lead a person away from the claimed invention.

For the foregoing reasons, Applicant contends that the claimed invention is not obvious over the Kearney patent, and accordingly, respectfully request this rejection be withdrawn.

2. *Claims 1, 5, 10-15, 18, 22-27, 30, 31, 36-38, 42, 46, 47, 50, 51, 56-58, and 61 Are Not Rendered Obvious by the Kearney Patent in view of Aviv et al.*

The Action rejects claims 1, 5, 10-15, 18, 22-27, 30, 31, 36-38, 42, 46, 47, 50, 51, 56-58, and 61 as being unpatentable over the Kearney patent as applied to claims 1, 5, 10-15, 18, 22-26, 30, 31, 36-38, 42, 46, 47, 50, 56-58, and 61, and further in view of Aviv *et al.* ("Aviv reference"). The Action admits that the Kearney patent fails to teach the isolation and purification of mRNA using cellulose, but argues that the Aviv reference teaches the isolation of poly(A)-rich RNA by binding it to poly(dT)-cellulose, poly(U)-cellulose, or nitrocellulose fibers. It further contends that the ordinary skilled artisan would be motivated to use a stabilizing agent such as TMAC or TEAC in order to facilitate hybridization between the poly(A) RNA and the immobilized poly(T) molecule and provide for a simplified sample preparation. Because the use of poly(U)-cellulose or poly(T)-cellulose to isolate poly(A) RNA has been known in the art for more than 30 years , it concludes that it would have been obvious to those of ordinary skill in the art to isolate poly(A)RNA using a structural composition such as cellulose and stabilizing compositions such as TMAC and TEAC. Applicant respectfully traverses this rejection.

As discussed above, the Kearney patent does not teach an element of the claimed invention. It does not describe or teach the use of TEAC or TMAC for isolating poly(A) mRNA. The Aviv reference has been available since 1972. As argued above, if the invention were

obvious, why had no one combined TEAC or TMAC with the poly(T)-cellulose or poly(U)-cellulose chromatography methods of Aviv?

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2143.01 citing *In re Mills,* 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). There is no suggestion to combine the Aviv reference and the Kearney patent. While a person of ordinary skill in the art would want an improved method for isolating poly(A) mRNA, there is no teaching in either reference of how to achieve that by practicing the claimed method. Also as discussed above, one of ordinary skill in the art would not consider using TMAC or TEAC to reduce rRNA contamination, particularly because the Kearney patent shows how effective those agents are for hybridizing rRNA. One cannot ignore that portion of the Kearney disclosure. The Federal Circuit has stated, "It is impermissible within the framework of 35 U.S.C. § 103 to pick and choose from any on reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.,* 230 U.S.P.Q. 416 (Fed. Cir. 1986).

Based on the foregoing arguments, it is clear the claims are not rendered obvious by the cited references. Accordingly, Applicant respectfully requests this rejection be withdrawn.

3. *Claims 1, 5, 10-15, 18, 22-27, 30, 31, 36-38, 42, 46, 47, 50, 51, 56-58, and 61 Are Not Rendered Obvious by the Kearney Patent in view of Jacobs et al.*

The Action rejects claims 1, 5, 10-15, 18, 22-27, 30, 31, 36-38, 42, 46, 47, 50, 51, 56-58, and 61 as being unpatentable over the Kearney patent as applied to claims 1, 5, 10-15, 18, 22-26, 30, 31, 36-38, 42, 46, 47, 50, 56-58, and 61, and further in view of Jacobs *et al.* ("Jacob reference"). The Action admits that the Kearney patent fails to teach the use of sodium citrate,

but argues that the Jacobs reference teaches the use of sodium citrate to anneal oligonucleotides with TEAC or TMAC to increase the stability of the duplexes (page 4640). It also contends that one would have been motivated to use 1) sodium citrate solutions to anneal the poly(A) RNA with the poly(T) molecule given the routine nature of the technique in the art and 2) TEAC or TMAC in order to stabilize the hybridization between the poly(A) RNA and the poly(T) molecule. The Action concludes that it would have been *prima facie* obvious to those of ordinary skill in the art to use sodium citrate, which allegedly facilitates the annealing of nucleic acids, TMAC or TEAC as stabilizing compositions, and a structure to which poly(T) or poly(U) is attached. Applicant respectfully traverses this rejection.

The previous arguments pertain equally to this rejection. Neither the Kearney reference nor the Jacobs reference discloses or discusses isolation of poly(A) mRNA, and thus, an element of the claimed methods is absent. Jacobs is concerned with oligonucleotide duplexes and does not mention mRNA or poly(A) RNA, which is recited in the claims. Consequently, a proper *prima facie* obviousness rejection has not been lodged. Furthermore, even if a reference that did describe the use of mRNA or poly(A) RNA was cited in this rejection, there would be no motivation to combine these references together for the reasons described above. Accordingly, Applicant respectfully requests this rejection be withdrawn.

4. Claims 1, 5, 10-15, 18, 22-26, 30, 31, 36-38, 42, 46, 47, 50, 56-58, and 61 Are Not Rendered Obvious by the Kearney Patent in view of Conlan et al.

The Action rejects claims 1, 5, 10-15, 18, 22-26, 30, 31, 36-38, 42, 46, 47, 50, 56-58, and 61 as being unpatentable over the Kearney patent as applied to claims 1, 5, 10-15, 18, 22-26, 30, 31, 36-38, 42, 46, 47, 50, 56-58, and 61, and further in view of Conlan *et al.* ("Conlan reference"). The Action states that the Kearney patent teaches the use of SDS as a detergent, but

fails to teach the use of CHAPS or Triton X-100 detergents. It then contends that the Conlan reference teaches both detergents (abstract). The Action asserts that a person of skill in the art would have been motivated and had a reasonable expectation of success of substituting CHAPS or Triton X-100 for SDS. As such, the Action alleges, it would have been obvious to one of ordinary skill in the art to use detergents such as Triton X-100 and CHAPS. Applicant respectfully traverses this rejection.

Similarly, the combination of the Kearney patent and the Conlan reference does not support a *prima facie* obviousness rejection. Neither reference discusses poly(A) RNA or mRNA and thus, it would not be obvious to use these references to practice the claimed methods. Applicant respectfully requests this rejection be withdrawn.

D. Claims 7-9 and 60 Are Not Indefinite

The Action rejects claims 7-9 and 60 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. The Action contends that these claims recite a trademarked compound, which, according to MPEP § 2173.05(t) (citing *Ex Parte Simpson*, 218 U.S.P.Q. 1020 (B.P.A.I. 1982)), does not comply with § 112, second paragraph. Applicant respectfully traverses this rejection.

The MPEP states: "The presence of a trademark or trade name in a claim is **not**, *per se*, improper under 35 U.S.C. § 112, second paragraph. . . ." MPEP §2173.05(u). The Action does not identify why the use of Triton X-100 in the rejected claims is problematic. The use of Triton X-100 is fully described in the specification, for example, at page 7. Furthermore, Applicant notes that a search of the U.S.P.T.O.'s patent database indicates there have been 96 patents issued since 1976 in which the term "Triton X-100" appears in a claim. Accordingly, Applicant

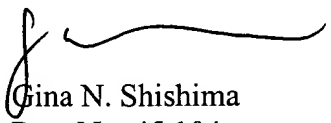
contends the claims satisfy § 112, second paragraph and respectfully request this rejection be withdrawn.

CONCLUSION

Applicant believes that the foregoing remarks fully respond to all outstanding matters for this application. Applicant respectfully requests that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is respectfully requested.

Respectfully submitted,



Gina N. Shishima
Reg. No. 45,104
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201
(512) 536-4598 (facsimile)

Date: May 14, 2003

APPENDIX A:

Claim Amendments Shown

1. (Amended) A method for purifying poly(A) mRNA [RNA] from a sample comprising:

a) incubating a composition comprising:

i) the sample, wherein the sample includes poly(A) mRNA;

ii) a poly(dT) or poly(U) nucleic acid molecule; and

iii) an isostabilizing agent, wherein the isostabilizing agent is tetramethylammonium chloride (TMAC) or tetraethylammonium chloride (TEAC),

under conditions allowing poly(A) mRNA [RNA] to hybridize with the [poly(T)] poly(dT) or poly(U) nucleic acid molecule; and

b) isolating the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA [RNA].

13. (Amended) The method of claim 1, further comprising washing the [poly(T)] poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA [RNA] in wash solution comprising an isostabilizing agent.

14. (Amended) The method of claim 13, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA [RNA] are washed more than once.

17. (Amended) The method of claim 14, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA [RNA] are washed at least once in a wash solution with an isostabilizing agent concentration greater than about 1.2 M and at least once in a wash solution with an isostabilizing agent concentration of less than about 0.5 M.

20. (Amended) The method of claim 18, further comprising isolating the non-reacting structure linked to the oligonucleotide that is hybridized to poly(A) mRNA [RNA].

24. (Amended) The method of claim 23, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA [RNA] are isolated from the sample with a magnet.

26. (Amended) The method of claim 18, further comprising eluting the poly(A) mRNA [RNA] from the non-reacting structure with an eluting solution of low ionic strength.

29. (Amended) The method of claim 28, further comprising

c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and

d) eluting the poly(A) mRNA [RNA] from the non-reacting structure with an eluting solution.

31. (Amended) A method for purifying poly(A) mRNA [RNA] from a sample comprising:

a) incubating the sample with a poly(dT) oligonucleotide connected to a non-reacting structure and a hybridization solution comprising tetramethylammonium under conditions allowing poly(A) mRNA [RNA]to hybridize with the oligonucleotide;

b) isolating the oligonucleotide with the hybridized poly(A) mRNA [RNA] away from the sample; and

c) washing the oligonucleotide with a wash solution comprising a salt.

34. (Amended) The method of claim 33, further comprising

c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and

d) eluting the poly(A) mRNA [RNA] from the non-reacting structure with an eluting solution.

35. (Amended) The method of claim 34, further comprising isolating the non-reacting structure linked to the oligonucleotide hybridized to poly(A) mRNA [RNA] by centrifugation or filtration.

36. (Amended) The method of claim 31, further comprising eluting the poly(A) mRNA [RNA] from the non-reacting structure with an eluting solution with low ionic strength.

APPENDIX: B

Pending Claims as of Response to Office Action Dated January 30, 2003

1. A method for purifying poly(A) mRNA from a sample comprising:

    a) incubating a composition comprising:

        i) the sample, wherein the sample includes poly(A) mRNA;

        ii) a poly(dT) or poly(U) nucleic acid molecule; and

        iii) an isostabilizing agent, wherein the isostabilizing agent is tetramethylammonium chloride (TMAC) or tetraethylammonium chloride (TEAC),

    under conditions allowing poly(A) mRNA to hybridize with the poly(dT) or poly(U) nucleic acid molecule; and

    b) isolating the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA.

2. The method of claim 1, wherein the final concentration of the isostabilizing agent in the composition is between about 1.0 M and about 3.0 M.

3. The method of claim 2, wherein the final concentration of the isostabilizing agent in the composition is between about 1.2 M and about 2.4 M.

4. The method of claim 3, wherein the final concentration of the isostabilizing agent in the composition is between about 1.5 M and about 2.0 M.

5. The method of claim 1, wherein the isostabilizing agent is provided to the composition in a hybridization solution.

6. The method of claim 1, wherein the composition further comprises CHAPS in a final concentration between about 0.5% and about 2.0%.

7. The method of claim 1, wherein the composition further comprises Triton X-100.

8. The method of claim 7, wherein the concentration of Triton X-100 in the composition is between about 0.01% and about 0.1%.

9. The method of claim 5, wherein the hybridization solution further comprises Triton X-100.

10. The method of claim 1, further comprising heating the composition at a temperature between about 70°C and about 90°C prior to incubation under hybridization conditions.

11. The method of claim 1, wherein the hybridization conditions comprise incubating the composition between about 15°C and 50°C for at least 10 minutes to 48 hours.

12. The method of claim 11, wherein the incubation time is at least 4 hours.

13. The method of claim 1, further comprising washing the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA in wash solution comprising an isostabilizing agent.

14. The method of claim 13, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA are washed more than once.

15. The method of claim 13, wherein the isostabilizing agent is TMAC or TEAC.

16. The method of claim 15, wherein the concentration of the isostabilizing agent in the wash solution is between about 0.05 M and about 3.0 M.

17. The method of claim 14, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA are washed at least once in a wash solution with an isostabilizing

agent concentration greater than about 1.2 M and at least once in a wash solution with an isostabilizing agent concentration of less than about 0.5 M.

18. The method of claim 1, wherein the poly(dT) or poly(U) nucleic acid molecule is linked to a non-reacting structure.

19. The method of claim 18, wherein the non-reacting structure is cellulose.

20. The method of claim 18, further comprising isolating the non-reacting structure linked to the oligonucleotide that is hybridized to poly(A) mRNA.

21. The method of claim 20, further comprising washing the non-reacting structure.

22. The method of claim 18, wherein the non-reacting structure is a bead.

23. The method of claim 22, wherein the bead is magnetic.

24. The method of claim 23, wherein the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) mRNA are isolated from the sample with a magnet.

25. The method of claim 20, wherein the non-reacting structure is isolated from the sample by centrifugation or filtration.

26. The method of claim 18, further comprising eluting the poly(A) mRNA from the non-reacting structure with an eluting solution of low ionic strength.

27. The method of claim 26, wherein the eluting solution comprises sodium citrate.

28. The method of claim 1, wherein the poly(dT) or poly(U) nucleic acid molecule is biotinylated.

29. The method of claim 28, further comprising

c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and

d) eluting the poly(A) mRNA from the non-reacting structure with an eluting solution.

30. The method of claim 1, wherein the sample or the hybridization solution does not contain guanidinium.

31. A method for purifying poly(A) mRNA from a sample comprising:

a) incubating the sample with a poly(dT) oligonucleotide connected to a non-reacting structure and a hybridization solution comprising tetramethylammonium under conditions allowing poly(A) mRNA to hybridize with the oligonucleotide;

b) isolating the oligonucleotide with the hybridized poly(A) mRNA away from the sample; and

c) washing the oligonucleotide with a wash solution comprising a salt.

32. The method of claim 31, wherein the non-reacting structure is cellulose.

33. The method of claim 31, wherein the oligonucleotide is biotinylated.

34. The method of claim 33, further comprising

c) incubating the biotinylated oligonucleotide and the sample with avidin or streptavidin linked to a non-reacting structure; and

d) eluting the poly(A) mRNA from the non-reacting structure with an eluting solution.

35. The method of claim 34, further comprising isolating the non-reacting structure linked to the oligonucleotide hybridized to poly(A) mRNA by centrifugation or filtration.

36. The method of claim 31, further comprising eluting the poly(A) mRNA from the non-reacting structure with an eluting solution with low ionic strength.

37. A kit, in a suitable container means, comprising:

a) a poly(dT) oligonucleotide linked to a non-reacting structure; and

b) binding solution comprising an isostabilizing agent.

38. The kit of claim 37, wherein the isostabilizing agent in the binding solution is TMAC or TEAC.

39. The kit of claim 38, wherein the concentration of TMAC or TEAC in the binding solution is between about 1.0 M and about 5.0 M.

40. The kit of claim 39, wherein the concentration of TMAC or TEAC in the binding solution is about 4.0 M.

41. The kit of claim 39, wherein the concentration of TMAC or TEAC in the binding solution is about 2.0 M.

42. The kit of claim 37, wherein the binding solution further comprises at least one detergent.

43. The kit of claim 42, wherein the detergent is Triton X-100 or CHAPS, or a combination of Triton X-100 and CHAPS.

44. The kit of claim 43, wherein the concentration of the detergent in the binding solution is between about 0.001% to about 1.0%.

45. The kit of claim 37, further comprising a detergent in a concentration of between about 0.01% and 0.1%.

46. The kit of claim 37, further comprising a wash solution comprising an isostabilizing agent.

47. The kit of claim 46, wherein the isostabilizing agent in the wash solution is TMAC or TEAC.

48. The kit of claim 47, wherein the concentration of TMAC or TEAC in the wash solution is between about 0.1 M and about 2.0 M.

49. The kit of claim 48, wherein the concentration of TMAC or TEAC in the wash solution is about 2.0 M.

50. The kit of claim 37, further comprising an elution solution of low ionic strength comprising a chelating salt.

51. The kit of claim 50, wherein the salt in the elution solution is sodium citrate or EDTA-2Na.

52. The kit of claim 50, wherein the concentration of the salt in the elution solution is between about 0.1 mM and about 100 mM.

53. The kit of claim 37, wherein the oligonucleotide is biotinylated.

54. The kit of claim 53, wherein the non-reacting structure is a streptavidin or avidin matrix.

55. The kit of claim 37, wherein the non-reacting structure is cellulose.

56. The kit of claim 37, wherein the non-reacting structure is a bead.

57. The kit of claim 56, wherein the bead is magnetic.

58. The kit of claim 57, further comprising a magnetic stand.

59. The kit of claim 37, further comprising a filtration device.

60. A kit, in suitable container means, comprising:

a) a poly(dT) oligonucleotide linked to cellulose;

b) hybridization solution comprising tetramethylammonium (TMAC) in a concentration of between about 1.2 M and about 4 M and Triton X-100 in a concentration of between about 0.03% and about 0.1%;

c) a first wash solution comprising TMAC in a concentration of about 2 M;

d) a second wash solution comprising TMAC in a concentration of about 0.4 M; and

e) elution solution having a total ionic strength of less than 0.01.

61. The method of claim 1, wherein the isostabilizing agent is TMAC, and wherein the nucleic acid molecule is poly(dT) and is linked to a non-reacting structure, and further comprising c) washing the poly(dT) nucleic acid molecule with a wash solution comprising a salt.